REMARKS

Claims 17-44 are pending. Claim 17 is currently amended.

Rejection for nonstatutory double patenting

The nonstatutory double patenting rejection over Matson (U.S. 6,787,040) in view of Kotitschke and Hoffman. is rendered moot by applicant's submission herewith of a terminal disclaimer.

Rejections under 35 U.S.C. §103

The combination of Matson and Ash is precluded under 35 U.S.C. §103(c) and does not provide all the limitations of independent claim 17

The office action rejected claims 17-23 as obvious over Matson (U.S. Patent No. 6,287,516) in view of Ash (U.S. Patent No. 5,919,369).

Applicants note that under 35 U.S.C. §103(c), the Matson reference can not be used to preclude patentability because at the time the claimed invention was made, the subject matter of the Matson reference was owned or subject to an obligation of assignment by the same person, Immunocept L.L.C.

Even if the Matson reference were available as prior art, in order to establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Because Ash does not provide the limitation of a hemofilter with a molecular weight cutoff of greater than 150,000 and less than 1,000,000, each limitation of currently amended claim 17 is not taught. Because independent claims 18 to 23 are dependent on claim 17, these claims are patentable for at least the same reasons.

It would not have been obvious to one of ordinary skill in the art at the time of filing to use a hemofilter having a molecular weight cutoff of greater than 150,000 Daltons and less than 1,000,000 as required by independent claim 17. Ash does not teach such a hemofilter;

the office action misunderstands the Ash reference. The passage of Ash recited in the office action to support this purported teaching is Column 7, lines 4-8 and 14-16. Read in context, this passage points out that "there are many suitable hollow fiber filter membranes which are known for use in **plasmafiltration or hemofiltration** ..." (emphasis added). Accordingly, the filters cited in this paragraph fall into two categories: plasma filters and hemofilters. It is known in the art that **plasmafiltration** requires a filter with a molecular weight cutoff (MWCO) that that is much greater than required for **hemofiltration**. The functional difference is pointed out by Ash in the same paragraph, which states "Such membranes...will have pore sizes sufficiently large to allow passage of proteins (e.g., in **plasmafiltration**) and/or middle molecular weight blood toxins (e.g., in **hemofiltration**)." (emphasis added).

Moreover, it is known in the art that plasmafilters employ large pores that exclude all but the largest blood components (e.g., blood cells). Plasmafilters are useful for plasmapheresis, the separation of plasma (including large molecules such as antibodies) from whole blood. Indeed, the example of a plasmafilter given by Ash is the Plasmaflo AP-05H (L), which Ash claims has a MWCO of "about 1,000,000" (same paragraph, lines 16 and 22).

By contrast, the specific examples of hemofilters given by Ash disclose molecular weights of 50,000; 60,000; and 70,000. Thus, there is a difference of **930,000 Da** between the most porous hemofilter disclosed and the single plasmafilter disclosed. Accordingly, it is incorrect to read the passage at column 7, line 10 which recites "50,000 to 6,000,000" as teaching the use of any filter with a molecular weight cutoff of greater than 150,000 because it simply encompasses the range of molecular weight cutoffs spanning two distinct classes of filters: hemofilters, which were contemplated by Ash to have MWCO values in the range of 50,000 to 70,000, and plasmafilters, with a MWCO of about 1,000,000. To reiterate, Ash teaches "plasmafiltration **or** hemofiltration" (emphasis added), not the use of a filter having a MWCO in the intermediate range.

In evidence, Ash teaches away from the presently claimed invention. Ash recommends that his invention be used for "hemofiltration wherein **middle molecular weight** molecules (i.e., having molecular weights of about **300 to 10,000**) are filtered across a membrane)..." (column 5, lines 17-19, emphasis added). In contrast, the presently claimed invention teaches the filtration of target-complex molecules (e.g.,, albumin bound to a toxin) using a filter having a MWCO of greater than 150,000 Da. For example, albumin, even

without being complexed, has a molecular weight of approximately 66,000 Da, which is almost **7-fold high**er than the largest "middle weight" toxin disclosed by Ash.

While it is true that the present invention may also allow the removal of molecules having molecular weights of about 300 to 10,000, as set forth in claim 17, this is only a superficial similarity in function without a correlate in structure. The present invention performs this function in a different and potentially more efficacious way: it allows the passage of target receptor complexes such as albumin-toxin complexes through the pores of a hemofilter having a MWCO of greater than 150,000 Da. Ash, however, circulates a sorbent containing solution (preferably activated charcoal) that binds small molecules that have passed across the pores of a protein-retaining filter.

In addition, the use of hemofilters that pass proteins such as albumin is not enabled by Ash. If such a filter was used as the hollow fiber filter (e.g. 107 of Fig. 4), then large amounts of protein would foul the sorbent-containing dialysis system. Moreover, the patient would be depleted of albumin and other molecules, and would lose oncotic pressure. Therefore, a more natural interpretation of the role of the plasmafilter in Ash is that the use of this component is part of the hemoglobin detection system for detecting blood leaks. See Ash column 14, lines 23-25: "A hemoglobin detection system (for detecting blood leaks) is provided by plasma filter 138…"

The combination of Ash and Davidner does not provide all the limitations of independent claim 17.

The office action also rejects claims 17-23 over Ash in view of Davidner. However, Ash is again misunderstood here. All of the limitations of independent claim 17 are not taught by this combination.

The office action (page 5, 2nd full paragraph) purports that Ash teaches a "large pore or very large pore hemofilter". This terminology does not appear in Ash but "very large pore" is a term used by the applicants in the present application. To use the applicant's own disclosure against them in this way constitutes impermissible hindsight and is improper. "To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used

against its teacher." *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 USPQ 303, 312-313 (Fed. Cir. 1983). Furthermore, these terms are not limitations of independent claim 17, which, as amended, requires a "blood filter having a nominal molecular weight cutoff of greater than 150,000 and less than 1,000,000 Daltons." As discusses above with reference to the Matson/Ash combination, this limitation is not taught by Ash.

With regard to the "source," the office actions purports that Ash teaches this at column 8, lines 8-14, and column 9, lines 2-12 and 31-33. However it is entirely unclear which feature of the Ash device is referred to in this rejection. Claim 17 of the present invention requires "a source for infusing a replacement fluid into the blood circuit, the source including replacement fluid comprising clean target receptor molecules...," a limitation that is not taught by Ash. The applicants are not aware of any such teaching by Ash and the examiner is invited to particularly point out a feature of Ash with respect the figures or text that corresponds to this clause of claim 17. Furthermore, because Ash teaches the removal of toxins in the range of 300 to 10,000 Da through dialysis and binding to a sorbent, a functional scheme that is substantially different from the hemofiltration scheme of the present invention, Ash would not have required such a source.

Neither does Davidner provide the missing limitations. Because all of the limitations are not found in the prior art, the invention is not obvious under 35 U.S.C. §103. Dependent claims 18-23 are patentable for at least the same reasons.

The combination of Ash, Davidner, and Kotitschke does not provide all the limitations of independent claim 24, no teaching, suggestion, or motivation to combine is offered, and the combination would render Ash unsuitable for its intended use.

The office action rejected method claims 24-29 and 31-44 over Ash in view of Davidner and Kotitschke (U.S. Patent No. 4900,720). Of note, the office action alleges that Ash teaches the use of large and very large pore hemofilters having MWCOs ranging from below 150,000 up to 1,000,000. As discussed above, this represents a misstatement of what Ash teaches. To the contrary, Ash discloses a sorbent-based dialysis (as opposed to hemofiltration) system that uses hemofilters having a MWCO of 50,000 to 70,000, with an embodiment that includes a plasmafilter as part of a leak sensing unit (item 138).

Additionally, the office action purports that Ash discloses a hemofilter 128 operable to produce a stream of ultrafiltrate. This is incorrect, hemofilter 128 is used in dialysis mode; i.e. a dialysis fluid is pumped across the outside of the hollow fibers. In contrast the invention demarked by claim 24, involves the creation of a hemofiltration stream. A hemofiltration stream differs from a dialysis stream in that the fluid carried in the hemofiltration is generated predominantly from the patient's blood in response to the urging of blood through the hemofilter. To illustrate a functional difference, if the flow of blood through the hemofilter were to stop, the hemofiltration system used in the method of claim 24 would generate little or no ultrafiltrate. However, a similar cease of blood flow through the dialysis system of Ash would not substantially affect the flow of dialysis fluid outside of the hollow fibers.

The office action maintains that Ash teaches a source for infusing replacement fluid and that compositions contained in the source are accorded little patentable weight. Applicants note that independent claim 24 does not require a "source" and that the present claims are for a method that requires "providing a fluid, containing clean target receptor molecules, to the patient." The examiner is invited to point out a statutory or administrative basis for such an assertion.

Furthermore, no appropriate teaching, suggestion or motivation to combine the Ash and Davidner references is offered in the office action. The office action provides the following justification for combining these references: "to have modified the Ash system by designing the hemofilter and circuit to form flow of ultrafiltrate and flow of filtered fluid in such manner to effect such ultrafiltration rates, to maintain system blood pressure, simplify the circuit, and prevent septimia (sic) conditions." The Ash system is not an ultrafiltration system, and no proper motivation is provided here for modifying it to become one. One cannot increase an ultrafiltration rate where none exists to begin with. Additionally, it is not clear how or why the proposed benefits of maintaining the system blood pressure, simplifying the circuit or preventing septicemia are lacking from Ash or improved through the teachings of Davidner. This merely conclusory statement constitutes impermissible hindsight. See, *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 220 USPQ 303, 312-313 (Fed. Cir. 1983).

The proposed modification of re-plumbing the Ash device to become a hemofilter based on Davidner would render Ash unsuitable for its intended use, dialysis of blood against a circulating sorbent. If a proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there is no suggestion or motivation to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). Such is the case here; including the circulating sorbent in the fluidic system of Davidner would be disastrous. For example, if the sorbent were included in the reservoir (item 209 in Fig 1 of Davidner), the sorbent would clog one or both of the filters (the charged fabric filter 111, and the 10 kDa filter 112). Even if the sorbent particles could pass through the filters, the sorbent would then pass to the patient's vasculature and almost certainly cause an embolism or other untoward result. A related problem would occur if a filter in the claimed MWCO range were to be substituted for the filter of Davidner; albumin and other large proteins would occlude one or more of the filters 111 and 112. Note that the Davidner system is designed with a hemoconcentrator 106 that excludes plasma proteins including albumin (see, e.g., column 6, line 3-5 and column 7, lines 15-18).

For at least the foregoing reasons, applicants submit that all claims pending in the application are allowable over the art of record. Early notice to that effect is respectfully solicited. Reconsideration of the application and issuance of a notice of allowance are respectfully requested. It is believed that no extension of time is required, but Applicants hereby petition for and request that any extension or other fee required for timely consideration of this application be applied and charged to Deposit Account No. 19-4972. The Examiner is requested to telephone the undersigned if any matters remain outstanding so that they may be resolved expeditiously.

Respectfully submitted,

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